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- 1) General Transmittal Letter (in duplicate);
- 2) Reply Brief;
- 3) Return Postcard.

Jane Massey Licata

08-20-02 AF/1600 AUS '1 6 2002 TRANSMITTAL LETTER Docket No. (General - Patent Pending) ISPH-0463 In Re Appleation Of: Monia et al. Filing Date Examiner Group Art Unit Serial No. 1655 J. Fredman 09/575,554 May 22, 2000 ANTISENSE OLIGONUCLEOTIDE INHIBITION OF RAS Title: AUG 2 2 2002 TECH CENTER 1600/2900 TO THE ASSISTANT COMMISSIONER FOR PATENTS: Transmitted herewith is: Reply Brief; Certificate of Express Mailing via Express Mail Label No. EV157158074US; and Return Postcard. in the above identified application. X No additional fee is required. A check in the amount of is attached. The Assistant Commissioner is hereby authorized to charge and credit Deposit Account No. 50-1619 \boxtimes as described below. A duplicate copy of this sheet is enclosed. Charge the amount of \boxtimes Credit any overpayment. \boxtimes Charge any additional fee required. Dated: August 16, 2002 Jane Massey Licata, Reg. No. 32,257 Licata & Tyrrell P.C. I certify that this document and fee is being deposited 66 East Main Street with the U.S. Postal Service as Marlton, NJ 08053 first class mail under 37 C.F.R. 1.8 and is addressed to the

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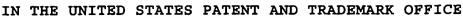
Assistant Commissioner for Patents, Washington, D.C. 20231.

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Attorney Docket No.:

ISPH-0463

AUG 2 2 2002

Inventors:

Monia et al.

Serial No.:

09/575,554

TECH CENTER 1600/2900

Filing Date:

May 22, 2000

Examiner:

Jeffrey Norman Fredman

Group Art Unit:

1637

Title:

Antisense Oligonucleotide Inhibition of

RAS

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By Jane Massey Licata, Reg. No. 32,257

U.S. Patent & Trademark Office

P.O. Box 2327

Arlington, VA 22202

Dear Sir:

REPLY BRIEF

This is in reply to the Examiner's Answer mailed July 12, 2002.

I. Status of Claims

Appellants acknowledge that the obviousness-type double patenting rejection of the claims has been withdrawn in response to the terminal disclaimer filed on February 11, 2002.

II. Grouping of Claims

Appellants respectfully point out that the Appeal Brief as filed included a statement indicating that claims 1 and 7-20 would fall or stand together (see page 4 of the Brief as filed).

III. Response to the Examiner's Arguments

The Examiner suggests that Appellants have not identified any specific limitation which is missing in the rejection. Appellants respectfully point out that at pages 6-8, and in particular at page 8, of the Appeal Brief mailed on May 20, 2002 the specific limitation not taught by the cited prior art is clearly identified. This limitation is the recitation of specific sequences for antisense compounds to Ki-ras. As discussed in detail in Appellants' Brief, none of the references, including Bos et al., teach or suggest a specific sequence of an antisense compound targeted to Ki-ras as presently claimed. Therefore, Appellants respectfully submit that the cited combination of prior art fails to establish a prima facie case of obviousness as it fails to teach the claimed limitation, i.e., specific sequences of antisense

compounds targeted to Ki-ras. Therefore, this combination of art fails to meet the requirements for obviousness under 35 U.S.C. 103(a).

Appellants also respectfully disagree with the Examiner's suggestion that the cited art provides a reasonable expectation of success that the claimed specific antisense oligonucleotide sequences would successfully inhibit expression of Ki-ras. It is only with the specification in hand that one of skill has evidence of Ki-ras using antisense of successful inhibition oligonucleotides. Although there is similarity among the various ras genes, the art does not demonstrate inhibition of Ki-ras using antisense, and there is no teaching in any of the prior art cited of the antisense sequences as claimed.

Appellants also respectfully disagree with the Examiner's suggestion that the instant claims which recite "an oligonucleotide 8 to 30 nucleobases which comprises at least an 8-nucleobase portion" of an identified SEQ ID NO. is different than the language of the issued claim of U.S. Patent No. 6,117,848. The 6,117,848 patent claims "an oligonucleotide 8 to 30 nucleobases which comprises". The Examiner has cited another patent but Appellants' arguments are based on the 6,117,848 patent which was allowed by Examiner Fredman. As discussed in detail in the Appeal Brief, both claims use the open "comprising" language. Both claims are directed to portions of the cited sequences as small as 8

nucleobases. Appellants disagree with the Examiner's suggestion that the language of the 6,117,848 patent excludes (8 nucleobase portions) of the claimed sequences.

the respectfully that Appellants also point out unpredictability of the art of antisense is a consideration in this As discussed in the Appeal Brief, the data provided in the specification clearly showed that antisense instant oligonucleotides targeted to ras functioned in some cases to reduce expression while in the case of other antisense compounds targeted to the same regions, no such inhibition was seen (See Tables 2 and This fact demonstrates to one 11 of the specification as filed). of skill that since only certain antisense compounds targeted to ras had the ability to inhibit gene expression, success would not be expected based on the use of references showing activity to a target other than Ki-ras.

Respectfully submitted,

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Date: August 16, 2002

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